Remarks

Reconsideration of the instant Office Action, entry of the amendments submitted herewith, withdrawal of the rejection of the claims 1-3, 5, 7, 9, 11, 22, 30 and 33 and of the objection to claims 23, 24, 27 and 28, in view of the amendments and remarks presented herein, and allowance of claims 1-3, 5, 7, 9, 11, 22-24, 27, 28, 30 and 33 are respectfully requested.

In the instant Office Action, claims 1-43 are listed as pending, claims 4, 6, 8, 10, 12-21, 25, 26, 29, 31, 32 and 34-43 are listed as withdrawn from consideration, claims 1-3, 5, 7, 9, 11, 22, 30 and 33 are listed as rejected and claims 23, 24, 27 and 28 are objected to as being dependent upon a rejected base claim.

Claims 1, 22-24, 27 and 28 are amended and claims 4, 6, 8, 10, 12-21, 25, 26, 29, 31, 32 and 34-43 are canceled.

Claims 4, 6, 8, 10, 12-21, 25, 26, 29, 31, 32 and 34-43 are canceled solely in response to the restriction requirement and without prejudice to their presentation in an appropriately-filed divisional application.

The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claims 1-3, 5, 7, 9, 11, 22, 30 and 33 under 35 U.S.C. §112, First Paragraph, as the Specification fails to enable the imidazolyl derivatives of formulae I and II, other than those in which R^1 is hydrogen. The rejection is respectfully traversed.

In support of this rejection, the Examiner states that "[o]nly compounds wherein R^1 is hydrogen have been made." This statement is incorrect. Applicants' respectfully request that the Examiner refer to the Tables found on pages 71-320 of the present specification wherein the hplc retention time and mass spectra results, evidencing the manufacture of 13,776 examples according to the present

application, are provided. In particular, Applicants direct the Examiner's attention for the Tables for sub-formulae 5, 8, 12,15, 18, 21 and 22 wherein the moiety at R^1 is not hydrogen.

Applicants further submit that the Examiner failed to appreciated that the vast majority of the 13,776 examples disclosed in the present application were synthesized using combinational synthetic chemistry methods described as representative examples at the head of the Table of Compounds (*See* page 70). Applicants state that compounds of the instant invention were assessed for their biological activity. (*See*, page 26, lines 8-9), and, moreover, the specification provides exemplary *in vitro* assays (*See* pages 26-28) to identify whether a compound of the present invention exhibits an affinity to bind to a somatostatin subtype receptor. Thus, the Applicants have provided a disclosure sufficient to enable the art worker to practice the invention as broadly as it is claimed.

It is well settled that it is not necessary that a patent applicant have prepared and tested all the embodiments of his invention in order to meet the requirements of §112. In re Angstadt, 537 F.2d 498, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). If Applicant's invention is disclosed so that one of ordinary skill in the art can practice the claimed invention, even if the practice of the invention by the art worker includes routine screening or some experimentation, Applicant has complies with the requirements of 35 U.S.C. §112, first paragraph. In re Angstadt, 537 F.2d 498, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976).

With respect to the Examiner's rejection of claims 1 and 22 under 35 U.S.C. §112, first paragraph, based on the lack of support for the present compounds as "prodrugs",

Applicants respectfully submit that a skilled artisan would readily understand that the term "prodrug" refers to a composition or compound that, upon or after administration to a subject, is transformed into a compound of the claimed genus.

Indeed the term "prodrug" is widely employed in U.S. patents. A cursory review of the U.S.P.T.O. database for the years 1996-2002 indicate that the objectionable term appears in over 700 patents, and that in approximately 100 of the discovered patents, the term does not appear separately in the specification, i.e., is not separately defined.

Notwithstanding the foregoing and solely to facilitate expedient examination of the present application, Applicants now amend the claims to remove the objectionable term from claims 1 and 22, and by implication, the pending claims dependent thereon.

Withdrawal of the rejection of claims 1-3, 5, 7, 9, 11, 22, 30 and 33 under 35 U.S.C. §112, First Paragraph, is respectfully requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 1 and 22 under 35 U.S.C. §112, Second Paragraph, as being indefinite for "failing to particularly point out and distinctly claim the subject matter to which applicant (sic) regards as the invention" due to the ambiguity of the term "optionally substituted". The rejection is respectfully traversed. Applicants respectfully submit that a skilled artisan would readily understand that the term "optionally substituted" indicates the subject moiety may or may not be substituted, but that a substituted moiety is preferred.

Indeed the term "optionally substituted" is widely employed in U.S. patents. A cursory review of the

U.S.P.T.O. database for the years 1996-2002 indicate that the objectionable term appears in over 40,632 patents.

Notwithstanding the foregoing and solely to facilitate expedient examination of the present application, Applicants now amend the claims to remove the objectionable term from claims 1 and 22, and by implication, the pending claims dependent thereon.

The Examiner rejected claim 1 under 35 U.S.C. §112, Second Paragraph, as being indefinite for use of the term "pharmaceutically-acceptable salts" more than once in the same line. The rejection is respectfully traversed. The first use of the objectionable term is to indicate that the Applicants claim a pharmaceutically-acceptable salt of a prodrug of the novel compound. The second use of the objectionable term is to indicate that the Applicants claim a pharmaceutically-acceptable salt of the compound itself. Applicants' prior amendment to delete the objectionable term "prodrug" from claim 1 renders this objection moot.

Withdrawal of the rejection of claims 1 and 22 under 35 U.S.C. §112, Second Paragraph, is respectfully requested.

The 35 U.S.C. §103(a) Rejection

Applicants respectfully submit that WO98/27108 anticipates the genus of the present application when R^1, R^2 and R^6 are all H, R^3 is $-(CH_2)_m-E-(CH_2)_m-Z^2$ wherein the 1st occurrence of m = 0, E is a bond, the 2nd occurrence of m = 0 and Z^2 is H, R^4 is $-(CH_2)_m-A^1$ wherein m = 0 and A^1 is equal to X^2 with $X^2 = -(CH_2)_m-Y^1-X^3$ in which m = 0, Y^1 is C(O) and X^3 is one of (C_1-C_{12})alkyl, aryloxy, imidazolyl, benzothiazolyl, indolyl, benzo[b]furanyl, quinolinyl, substituted $-(CH_2)_m-$phenyl wherein m=0 and the phenyl substituted with NH_3 or lower alkyl, or pyrimidinyl, and R^5 is aryl. To remove this combination from the scope of the genus claim, Applicants have appended *proviso* (d) to claims 1 and 22.

With respect to Compound 27, it should be noted that said compound is not consistent with the formula I, the genus, of WO98/27108. Applicants respectfully disagree with the Examiner's position that Compound 27 is functionally identical to the compounds of the present application. The moiety that corresponds to position R^6 of genus of the present application for Compound 27, is a phenyl group substituted with Bromine. According to the definition of R^6 for the present application, R^6 can only be H or a lower alkyl. As such, Compound 27 is not within the scope of the genus of the present application. Applicants respectfully disagree with the Examiner's opinion that Compound 27 is a positional isomer, since the ***bond connectivity*** of Compound 27 and the genus of the present application are ***not identical.*** The Examiner is correct the position R^5 of the genus of the present application does allow for an aryl group substituted with Bromine. However, according to the genus of the present application, such a moiety must be situated between two carbon atoms of the heterocyclic ring. The bromide-substituted aryl of Compound 27, however, is bonded to a carbon and a ***nitrogen*** atom of the heterocyclic ring. As such, the lack of similar bond connectivity, which is a requirement for positional isomers, is not present and merely reversing R^5 and R^6 of Compound 27 would not be obvious.

Applicants demand that the Examiner provide a basis in the form of a treatise or other authority for his opinion that Compound 27 is a positional isomer of the present genus.

Even if WO98/27108 disclosed a positional isomer of a species of the claimed genus, there is no teaching or suggestion that the substituted aryl group could be switched

with the hydrogen on the imidazole ring of Compound 27, as is required under of 35 U.S.C. 103(a) rejection.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone the Applicants' attorney at the below-listed number to facilitate the prosecution of this application. If necessary, please charge any additional fees deemed necessary to Deposit Account 50-0590.

Respectfully submitted,

Date: 5-5-2003

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